19. Costanzo MR, Naftel DC, Pritzker MR, Heilman JK 3rd, Boehmer JP, Brozena SC, et al. Heart transplant coronary artery disease detected by coronary angiography: a multiinstitutional study of preoperative donor and recipient risk factors. Cardiac Transplant Research Database. *J Heart Lung Transplant*. 1998;17:744-53.
20. Mulla NF, Johnston JK, Vander Dussen L, Beeson WL, Chinnock RE, Bailey LL, et al. Late rejection is a predictor of transplant coronary artery disease in children. *J Am Coll Cardiol*. 2001;37:243-50.
21. Hussain T, Burch M, Fenton MJ, Whitmore PM, Rees P, Elliott M, et al. Positive pretransplantation cytomegalovirus serology is a risk factor for cardiac allograft vasculopathy in children. *Circulation*. 2007;115:1798-805.
22. Kuhn MA, Jutzy KR, Deming DD, Cephus CE, Chinnock RE, Johnston J, et al. The medium-term findings in coronary arteries by intravascular ultrasound in infants and children after heart transplantation. *J Am Coll Cardiol*. 2000;36: 250-4.
23. Pietra B, Boucek M. Coronary artery vasculopathy in pediatric cardiac transplant patients: the therapeutic potential of immunomodulators. *Paediatr Drugs*. 2003; 5:513-24.
24. Tissot C, Pietra BA, Ivy DD, Campbell DN, Mitchell MB, Diamond BA, et al. Transplant coronary artery disease is diagnosed later and is more severe in pediatric heart recipients transplanted during infancy [abstract]. *Cardiol Young*. 2009;20(Suppl 2):S24.

Discussion

Dr Jonathan Chen *(New York, NY).* I would like to congratulate Dr Karamichalis and colleagues from the Denver Children's Hospital on an impressive series from one of the leading centers for pediatric heart transplantation in North America.

While survival following transplantation continues to improve, regrettably a sizable minority of these recipients will require retransplantation and, in this way, transplantation is for many children a palliative procedure that merely postpones an inevitable graft replacement anywhere from several years to several decades following the primary operation.

Our findings at Columbia have mirrored those of Denver, suggesting that the survival outcomes following retransplantation are now comparable to primary transplantation in well-selected candidates. The report today seeks to further characterize this subcohort of retransplant candidates with a particular interest on the age at their primary procedure.

Having had, thank you, the benefit to review your data prior to this presentation, I have 4 questions for the authors.

The first is: Were there any children with graft failure who were not deemed retransplant candidates during your study period and thus did not make it into this study?

Dr Karamichalis. We had patients who were listed on the waiting list for retransplantation. We had 10 patients who were listed for retransplantation: 5 of them died on the transplant list, 2 of them were transferred to another facility, and 3 of them were removed from the list because their condition improved.

Dr Chen. Second, how was the decision made to divide these patients into groups that were greater than and less than 1 year of age? Inferences from ABO-incompatible strategies would suggest that the time of so-called immunologic privilege can extend as far as 14 months or longer.

Dr Karamichalis. Because of the known immaturity of the infant immune system, we felt that the infant recipient population would have an advantage over anybody over 1-year-old, so we divided the groups into less than 1 year or over 1 year. The ISHLT database registry divides these patients into more than 2 subgroups; however, because of our small group, we decided to draw the line between infants and older than 1.

Dr Chen. Third, I'm somewhat perplexed still at the finding that there is more transplant coronary disease but fewer incidences of rejection in your infant subcohort. And I wonder whether some of this could be due to the differences in surveillance that you describe with respect to your age-based protocols that dictate the timing of the endomyocardial biopsies.

Dr Karamichalis. The data concerning the short follow-up of those 5 patients corresponds to the time after retransplantation. All patients that had their first transplant and made it to retransplantation had surveillance angiograms at the first anniversary of their transplant and subsequently every other year. If there was evidence of CAV, then they would receive more frequent surveillance for CAV and treatments.

At the time of catheterization, all patients also had endomyocardial biopsies. So given the median graft survival of both the infant and the older group, the older being 3.9 years, then all of those patients should have at least had 2 or 3 endomyocardial biopsies and at least 3 angiograms.

Dr Chen. Do you know if it's the practice to treat episodes of transplant coronary disease in the absence of rejection? So could it be that the coronary disease was detected in the infants and they were treated before there was biopsy-proven rejection and thus the lower incidence of rejection?

Dr Karamichalis. Once CAV is diagnosed in these patients at our center, they get treated. And the strategy that we use, includes statins or antilipid agents, we also use MMF and rapamycin, an antiproliferative agent, to decelerate the progression of CAV in these patients. So any evidence or any signs of CAV, no matter how severe or mild they might be, they get treated. The treatment escalates based on the severity of the CAV.

Dr Chen. Finally, is it possible that the decreased graft survival and increased rejection in your group 2 was related to medication noncompliance, given that the fact that the average age of this group was 9, plus or minus 6 years, at their primary transplant, which would render many of them medically recalcitrant adolescents at the time of their initial post-transplant years.

Dr Karamichalis. I think that's an excellent point and it's definitely something worth mentioning. In the older population, there may be a compliance issue of which we are not aware. Even though we discussed it, we haven't really searched specifically for noncompliance in these patients, but it's definitely something that is well known to cause rejection in patients who don't take their medications.

Dr Chen. Thanks. These are very provocative and very interesting data. I'm very interested in how these findings play out as you follow these patients postretransplant.

Dr Carl Backer *(Chicago, Ill).* John, congratulations on a very nice analysis. Clearly, this is a huge amount of work.

I have a question. Given the data that you have on retransplantation, I'd like to ask your opinion about 2 high-risk groups. The first is the patient who has had their first transplant, doesn't come off bypass because they have right ventricular dysfunction, and now you're contemplating whether or not you should relist them for another transplant. Did you have any patients like that in your series and what are your thoughts about that population group?

Dr Karamichalis. Thank you for your comments and your question.

No, we did not have any relisting of early graft failure. One patient retransplanted was more than a year after his primary transplant. Everybody else got retransplanted at 2 or more years after their primary transplant. So I do not believe we have anybody that was relisted following primary transplantation with failure to come off bypass.

Dr Backer. The second question is: What do you think about a third-time transplant? Do you have any patients who you've transplanted a third time and what's your opinion about that?

Dr Karamichalis. I'm aware of 1 patient who was offered third-time retransplantation. That patient refused to be relisted and died subsequently of PTLD, which was unrelated to CAV or rejection. I know other centers have reported third-time retransplantations. I guess it would be a collective decision between everybody involved. And, if somebody makes a compelling case, then a third transplant should be offered but it would only be on a case-to-case basis.